REMARKS

Status of the Claims.

Claims 1-12, and 14-17 are pending with entry of this amendment, claims 13 and 18-32 being previously cancelled and no claims being added herein. Claim 1 is amended herein. This amendment introduces no new matter. Support is replete throughout the specification (*e.g.*, page 4, lines 18-20, and the like).

35 U.S.C. §112, first paragraph, written description.

Claims 1-12, and 14-17, were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner alleged that there is no corresponding sequence identifier for CYP24 nor is it clear form the claims that here is only one sequence of the candidate cancer marker. Applicants traverse.

It is well-accepted law that the description requirement of section 112 is met when "one of skill in the art would discern possession of the invention at the time of filing." As stated by the Court of Appeals of the Federal Circuit:

> After Enzo, this court recognized "that Ely Lilly did not hold that all functional descriptions of genetic material necessarily fails as a matter of law to meet the written description requirement, rather, **the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure**." Amgen, 314 F.3d at 1332, 1361 (dissent: "[T]he majority . . . verges on confining Ely Lilly to its facts.").
>
> In this case, as in Enzo, the court explained that the written description requirement is satisfied when "**one of skill in the art would discern possession of the invention at the time of filing**." [emphasis added] (Moba, B.V., Staalkat, B.V., And Fps Food Processing Systems, Inc., V. Diamond Automation, Inc., ___USPQ2d ___(Fed. Cir. 2003).

Moreover, "[t]he written description requirement **does not** require the applicant 'to describe exactly the subject matter claimed, [instead] **the description must clearly allow persons of ordinary skill in the art to recognize** that **[he or she] invented what is claimed.** [emphasis added]

'"*Union Oil Co. v Atlantic Richfield et al.* 208 F.3d 989 (Fed. Cir. 2000) *citing In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2D (BNA) 1614, 1618 (Fed. Cir. 1989). As stated by the Court:

> Appellant refiners assert that the specification does not describe the exact chemical component of each combination that falls within the range claims of the '393 patent. **However, neither the Patent Act nor the case law of this court requires such detailed disclosure.** See *In re Hayes Microcomputer Prods., Inc.*, 982 F.2d 1527, 1533, 25 U.S.P.Q.2D (BNA) 1241, 1245 ("[The applicant] does not have to describe exactly the subject matter claimed."); Vas-Cath, 935 F.2d at 1566 ("ranges found in applicant's claims need not correspond exactly to those disclosed in [the specification]; issue is whether one skilled in the art could derive the claimed ranges from the disclosure."). Rather, the Patent Act and this court's case law require only **sufficient description to show one of skill in the refining art that the inventor possessed the claimed invention at the time of filing.** **[emphasis added]**

In the instant case, claim 1 is directed to a method of detecting a predisposition to breast cancer in a human, where the method involves:

> (ii) detecting the level of CYP24 nucleic acid or CYP24 protein, within said biological sample, wherein said CYP24 nucleic acid or CYP24 protein is a nucleic acid or protein encoded by **the vitamin D 24 hydroxylase (CYP24) gene**; and

A brief Google Scholar search of articles published between 1980 and 1999 identified over 60 published references referring to CYP24 and describing the gene, its structure and regulation in substantial detail (*see, e.g.,* Exhibit A). These articles provide clear evidence that the vitamin D 24 hydroxylase (*CYP24*) gene was well known to those of skill in the art and that one of skill in the art clearly understood what was meant by a nucleic acid or protein encoded by the vitamin D 24 hydroxylase (CYP24) gene. . Moreover, as explained in the Applicants' previous response, and as evidenced by the publications in Exhibit A, one of skill in the art understood how to measure expression of the CYP24 gene.

Accordingly, in view of the extensive knowledge regarding the CYP24 gene and its thorough characterization, and even the GenBank numbers referenced in the specification, one of skill in the art would clearly recognize that Applicants were in "possession" of the claimed method.

Accordingly, the present application clearly complies with the written description requirement and the rejection of claims 1-12, and 14-17 under 35 U.S.C. §112, first paragraph, on these ground should be withdrawn.

35 U.S.C. §112, first paragraph, enablement rejection.

Claims 1-12 and 14-27 were rejected under 35 U.S.C. §112, first paragraph. The Examiner alleged that the specification does not ". . . provide enablement for a method of detecting a predisposition to any cancer. . . ". To expedite prosecution, claim 1 is amended herein to recite "[a] method of detecting a predisposition to **breast cancer** in a human . . . ".

The specification clearly identifies CYP24 as a **driver oncogene** for the amplicon at 20q13 (*see, e.g.,* Example 1), which amplicon has frequently been implicated in breast cancer.

The specification teaches a number of methods of detecting the CYP-24 gene or protein product. Thus, for example:

1) Example 1 of the present application teaches and illustrates the use of **RT-PCR to detect CYP-24 expression levels and provides PCR primers** to perform such RT-PCR.

2) Example 2 of the present application teaches **CYP-24 expression analysis using multi-color fluorescent in situ hybridization (mRNA-FISH)** on tissue sections.

3) Example 3 illustrates measurement of the **expression of CYP-24 at both the transcript and protein levels**.

Moreover, methods of detecting CYP24 amplification and/or expression were known to those of skill in the art. Thus, for example:

1) Jones *et al.* (1999) Expression and Activity of Vitamin D-Metabolizing Cytochrome P450s (CYP1α and CYP24) in Human Nonsmall Cell Lung Carcinomas, *Endocrinology*, 140(7): 3303-3310 (previously provided) **illustrates detection of CYP24 mRNA** using a Northern analysis.

2) Kerry *et al.* (1996) Transcriptional Synergism Between Vitamin D-responsive Elements in the Rat 25-Hydroxyvitamin D_3 24-Hydroxylase (*CYP24*) Promoter, *J. Biol. Chem.*,

271(47): 29715-29721 (previously) illustrates methods of detecting **induction of transcription of the CYP24 gene**;

There is simply no question that the present specification teaches that elevated CYP24 expression (*e.g.*, via amplification, overexpression, etc.) indicates a predisposition to breast cancer and teaches one of skill in the art how to perform the claimed method without undue experimentation. Accordingly, the rejection of claims 1-12 and 14-27 under 35 U.S.C. §112, first paragraph, should be withdrawn.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. **Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.**

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 267-4161.

BEYER WEAVER & THOMAS, LLP
500 12TH STREET, SUITE 200
OAKLAND, CA 94607
TEL: (510) 663-1100
FAX: (510) 663-0920

Respectfully submitted,

Tom Hunter
Reg. No: 38,498

C:_TOMS WORK_PROSECUTION - QUINELAW\407T UC OTT\407T-897900US\407T-897900US.AM7.DOC